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**Multidrug resistant and sensitive strains of *Pseudomonas aeruginosa*: Establishing clonal relationship by Pulsed Field Gel Electrophoresis and in vitro antibiotic synergy testing by E test.**

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**Background:** The emergence of multidrug resistant *Pseudomonas aeruginosa* (MDRPA) as one of the leading nosocomial pathogens imposes a serious health threat due to limited antibiotic options. In this study, a sample of clonally distinct MDRPA and sensitive strains of *Pseudomonas aeruginosa* (SSPA) were tested against various antibiotics combinations to establish synergistic activity against these strains.

**Methods:** A total of 39 retrospectively collected MDRPA strains isolated over three years with a particular antibiogram (sensitive to colistin but resistant to ceftazidime, cefepime, cefoperazone, cefoperazone/sulbactam, ciprofloxacin, imipenem, meropenem, piperacillin, piperacillintazobactam, gentamicin, netilmicin, with varying susceptibility to amikacin) and 19 SSPA collected prospectively were genotyped using *SpeI* DNA macrorestriction analysis and pulsedfield gel electrophoresis (PFGE). The strains were from different patients from various sites (blood, tissue, fluid, catheter tip, bronchiol alveolar lavage (BAL), urine, sputum, swab, tracheal secretion and nasal swab). Clonal relatedness was determined at  $\geq 85\%$  level of similarity and grouped into different clusters. A representative strain from each cluster was tested against 10 different paired combinations of various antimicrobials ( $\beta$ -lactams, quinolone, aminoglycoside, tigecycline, rifampicin and colistin) to establish synergistic activity against these strains using the investigational E test fixed ratio method.

**Results:** There were 46 distinct clones out of a total of 58 MDRPA and SSPA resolved by PFGE from which 10 clonally distinct strains (8 MDRPA and 2 SSPA strains) were selected for synergy testing. The antibiotic combination which most frequently demonstrated synergy was cefepime with amikacin (4/10 strains). Other synergistic combinations were aztreonam with either ceftazidime or cefepime, and meropenem with ciprofloxacin (3/10 strains respectively), ceftazidime with either ciprofloxacin or amikacin (2/10 strains respectively) and imipenem with ciprofloxacin (1/10 strains). The combination of ceftazidime with amikacin was antagonistic in 1/10 strains. The other antibiotics combinations were either additive or indifferent.

**Conclusion:** PFGE was a useful and discriminative molecular subtyping tool to establish clonal relatedness among strains. Results of antimicrobial synergy testing indicate that although certain combinations may act synergistically, it was still strain dependent. These preliminary findings require further confirmation with testing of a larger number of isolates.

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